Hypertriglyceridemia And Insulin Resistance is Associated with Hypothyroidism

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Abstract: Thyroid function regulates a wide array of metabolic parameters. Hypothyroidism is a very common endocrinopathy seen mostly in females. Dyslipidemia and insulin resistance have been demonstrated in hypothyroidism. The study group comprised of 50 hypothyroid patients and 50 age matched healthy controls. Serum samples of all the patients were assayed for thyroid profile, insulin, triglycerides and fasting blood glucose levels. Homeostasis model of assessment (HOMA-IR) was employed to assess the level of insulin resistance. Patients with hypothyroidism demonstrated insulin resistance and dyslipidemia as observed by the higher HOMA-IR and triglyceride levels respectively as compared to the controls. Thyroid dysfunction leads to alterations in glucose and lipid metabolism which is an important risk factor for diabetes and cardiovascular diseases. Regular monitoring of lipid and glucose levels in patients with thyroid dysfunction would be helpful in preventing cardiovascular diseases. The dyslipidemia and insulin resistance should be managed along with hormonal replacement to reduce the risk of atherosclerosis and further complications.

Keywords: Hypothyroidism, Insulin Resistance, Triglyceridemia, Dyslipidemia.

Introduction and Experimental:

Hypothyroidism is defined as a deficiency of thyroid activity, which results from reduced secretion of both T3 and T4 irrespective of the cause.1 It is the most common pathologic hormone deficiency among the endocrine disorders. Hypothyroidism may be due to primary disease of the thyroid gland itself or lack of pituitary TSH.2 Biochemically decrease in T4 and T3 concentrations lead to hypersecretion of pituitary TSH and an amplified increase in serum TSH levels. This is a key laboratory finding, particularly in the early detection of primary hypothyroidism. The prevalence of thyroid disease in patients with diabetes is significantly higher than that in the general population.3 This indicates a possible interplay between thyroid status and insulin sensitivity. Homeostatic model assessment (HOMA) is a method for assessing β-cell function and insulin resistance (IR) from basal (fasting) glucose and insulin or C-peptide concentrations. The homeostasis model assessment (HOMA) for insulin resistance (HOMA-IR) derives estimates of insulin sensitivity from the fasting plasma glucose and insulin concentrations. Insulin resistance augments the deleterious effect of hypothyroidism on the lipid profile as suggested by Bakker et al.4

The role thyroid hormones play in the regulation of plasma triglyceride (TG) concentration and transport, is not well known and relatively few studies have been carried out on the alterations of triglyceride and very low density lipoprotein (VLDL) metabolism in hypothyroid disease. The plasma triglyceride concentration may be completely normal in hypothyroidism but usually it is moderately elevated and occasional cases of gross hyperlipidemia have been reported in myxedema.5 6 7 This increase is attributed to a low lipoprotein lipase (LPL) activity.8
We aimed to investigate the relationship between insulin resistance, increased triglycerides in hypothyroid subjects attending a tertiary care hospital in Nellore, India.

The study was conducted in the department of Biochemistry, Narayana Medical College, Nellore. The patients visiting the Medical Endocrinology OPD at Narayana General Hospital, Nellore were screened and 50 patients suffering from subclinical and overt hypothyroidism were enrolled in the study after prior consent. Fifty age matched volunteers were enrolled as controls. All of them were in the age group of 20-40 years. Both males and females included.

Subjects in the age group of 20 to 40 years, newly diagnosed and untreated cases of hypothyroidism were included in the case group. Subjects having diabetes mellitus, PCOD, tuberculosis, other systemic illness, liver disorders, renal disorders, congestive cardiac failure, those taking oral contraceptive pills, statins and other medications that alter thyroid functions and lipid levels, pregnant and menopausal women, known cases of overt hypothyroidism or hyperthyroidism were excluded from the study. Pregnancy and menopause also accounted for exclusion from the study.

Sample collection and analysis:

The name, age and sex of the subjects were noted and about 5ml of venous blood sample was collected in the morning after 12 hours of an overnight fast after taking informed consent under aseptic conditions. Blood is allowed to clot; samples centrifuged at 2000 rpm (revolution per minute) for 10 minutes at room temperature. Serum is separated and stored at -20°C until the analysis, to minimize non-specific variability of all parameters. Plain tubes for serum, sodium fluoride, heparin for plasma were used.

Thyroid profile (TSH, FT3 and FT4) and insulin levels were estimated by chemiluminescence immuno assay using Beckman Coulter Access II using commercially available kits. Triglycerides (GPO-PAP method) and plasma glucose (glucose oxidase and peroxidase method(GOD-POD) were measured using reagent kits from Biosystem(Spain) using Humastare 300 chemistry analyser (Human GmbH Germany).

Homeostasis model assessment for insulin resistance (HOMA-IR) (mU∗millimol/liter²) was calculated as fasting insulin (mU/liter) times fasting glucose (mmol/liter) divided by 22.5.

Statistical Analysis

The statistical analysis was performed using IBM SPSS Version-20. Continuous data were expressed as Mean(SD). For statistical significance, a two tailed probability value of less than 0.05 was considered.

Results and Discussion

Table 1: Thyroid profile, Fasting blood glucose, Serum insulin in cases and controls

<table>
<thead>
<tr>
<th>parameters</th>
<th>CASES (n=50)</th>
<th>CONTROLS (n=50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH(mIU/ml)</td>
<td>19.6(14.59)</td>
<td>2.08(1.13)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>FT3(pg/ml)</td>
<td>2.58(0.71)</td>
<td>2.94(0.29)</td>
<td>0.001</td>
</tr>
<tr>
<td>FT4/ng/dl</td>
<td>0.51(0.28)</td>
<td>0.88(0.14)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>F.Glucose(mmol/L)</td>
<td>5.68(0.38)</td>
<td>5.45(0.28)</td>
<td>0.001</td>
</tr>
<tr>
<td>S.insulin(mIU/ml)</td>
<td>19.24(12.65)</td>
<td>5.38(1.48)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>4.93(3.3)</td>
<td>1.3(0.37)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Triglycerides(mg/dl)</td>
<td>158.44(65.61)</td>
<td>64.68(17.74)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data is expressed as mean (standard deviation). P <0.05 is considered significant.

TABLE 1 shows the mean values(SD) of the following parameters-TSH, FT3, FT4, Serum insulin, Fasting blood glucose, Serum triglycerides, and HOMA-IR. Normal range for TSH was (0.27–4.2) μIU/ml, FT3 was (2-4.4 pg/ml) and that for FT4 was (0.93–1.7) ng/dl. As compared to controls serum TSH value was significantly increased in hypothyroid patients [mean(SD) 19.6(14.59) vs 2.08(1.13) μIU/ml, P<0.0001]. Mean FT3 and FT4 in cases was decreased in cases compared to controls[P=0.001,P<0.0001 respectively]. The normal range for fasting insulin is taken as 2.6-24.9 μU/ml. The mean Fasting blood glucose and serum insulin in cases vs controls was [5.68(0.38) vs 5.45(0.28) mmol/L, P=0.001]; [19.24(12.65) vs 5.38(1.48), P<0.0001] respectively. Mean triglyceride values in cases and controls was

Thyroid disease is much more prevalent in women than men—women are five to eight times more likely to develop hypothyroidism.\(^9\) This is in accordance with our study showing a higher prevalence of hypothyroid status in females as compared to males. Hypothyroidism is one of the most common functional disorders of the thyroid gland. The condition can be identified by measuring the thyroid stimulating hormone (TSH) concentration in serum, which is elevated in the cases. Serum FT4 may or may not be decreased; these thyroid disorders are known as overt (OH) and sub-clinical hypothyroidism (SCH), respectively. SCH represents a condition of mild to moderate thyroid failure characterized by normal serum levels of thyroid hormones with mildly elevated serum TSH concentrations.\(^10,11\)

Thyroid hormones influence both production and removal of plasma triglycerides in man. In thyroid hypofunction, slight or moderate hypertriglyceridemia develops as a result of impaired removal of endogenous triglycerides, and the elimination of exogenous fat particles is also decreased.\(^6\) Hepatic triglyceride production was not diminished in severely hypothyroid subjects eventhough the plasma Free fatty acid levels were slightly less than in normal controls. This latter finding conforms with the observations on decreased sensitivity of adipose tissue of hypothyroid animals to lipolytic agents.\(^12,13\) In our study, serum triglycerides in cases were significantly elevated compared to controls.\(^P<0.0001\) Variations, generally, not very marked, observed in TG levels could be due to the action of thyroid hormone on VLDL. Earlier studies mirror the same findings.\(^14,15\)

The influence of thyroid hormone action on insulin levels and how insulin levels change in hypothyroid dysfunction has been studied extensively. The development of insulin resistance leads to many of the metabolic abnormalities and clinical hypothyroidism is associated with insulin resistance.\(^6\) The main pathophysiological basis underlying glucose intolerance, dyslipidemia, abdominal obesity and hypertension has been attributed to insulin resistance.\(^4\) Insulin resistance is a cardinal feature of type 2 diabetes mellitus and increased risk of dyslipidemia is frequently found in mild thyroid dysfunction.\(^1\)

HOMA IR was significantly raised in hypothyroid group as compared to controls.\(^P<0.0001\). Shantha et al have observed that females with insulin resistance have significant association with overt hypothyroidism.\(^16\) The relationship between glucose and insulin in the basal state reflects the balance between hepatic glucose output and insulin secretion, which is maintained by a feedback loop between the liver and \(\beta\)-cells. The use of HOMA to estimate insulin sensitivity and \(\beta\)-cell function helps to compare \(\beta\)-cell function and insulin sensitivity in subjects with abnormal glucose tolerance. Our study demonstrated that hypothyroidism leads to a state of insulin resistance. Maratouet al conducted a similar study and concluded that insulin resistance is associated with hypothyroidism.\(^7\)

Our study is limited by small sample size and referral bias. Population based studies are required to reinforce our study findings in a broader perspective. Despite these limitations, the associations we found were highly significant and consistent with other studies addressing similar association.

References

2. Shaikh Z, Thyroid related disorders at CHK. JCPSP, 1993, 3, 26-8


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